Amendments to Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Claim 1 (cancelled)

Claim 2 (cancelled)

Claim 3 (previously presented) A method to modulate the expression of one or more exogenous genes in a subject, wherein the subject is other than a plant, comprising administering to the subject an effective amount of a ligand of the formula:

$$\mathbb{R}^3 \longrightarrow \mathbb{R}^1$$

wherein:

E is a (C4-C5)alkyl containing a tertiary carbon or a cyano(C3-C5)alkyl containing a tertiary carbon;

R1 is H, Me, Et, i-Pr, F, formyl, CF2, CHF2, CHCl2, CH2F, CH2Cl, CH2OH, CH₂OMe, CH₂CN, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, OH, OMe, OEt, cyclopropyl, CF2CF3, CH=CHCN, allyl, azido, SCN, or SCHF2;

R² is H, Me, Et, n-Pr, i-Pr, formyl, CF₃, CHF₂, CHCl₂, CH₂F, CH₂Cl, CH₂OH, CH2OMe, CH2CN, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, Ac, F, Cl, OH, OMe, OEt, O-n-Pr, OAc, NMe2, NEt2, SMe, SEt, SOCF2, OCF2CF2H, COEt, cyclopropyl, CF₂CF₃, CH=CHCN, allyl, azido, OCF₃, OCHF₂, O-i-Pr, SCN, SCHF2, SOMe, NH-CN, or joined with R3 and the phenyl carbons to which R2 and R3 are attached to form an ethylenedioxy, a dihydrofuryl ring with the oxygen adjacent to a phenyl carbon, or a dihydropyryl ring with the oxygen adjacent to a phenyl carbon;

R⁹ is H, Et, or joined with R² and the phenyl carbons to which R² and R³ are attached to form an ethylenedioxy, a dihydrofuryl ring with the oxygen adjacent to a phenyl carbon, or a dihydropyryl ring with the oxygen adjacent to a phenyl carbon;

PAGE 3/12 * RCVD AT 3/7/2005 11:02:02 AM [Eastern Standard Time] * SVR:USPTO-EFXRF-1/5 * DNIS:8729306 * CSID:215 619 1665 * DURATION (mm-ss):03-22

R⁴, R⁵, and R⁶ are independently H, Me, Et, F, Cl, Br, formyl, CF₃, CHF₂, CHCl₂, CH₂F, CH₂Cl, CH₂OH, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, OMe, OEt, SMe, or SEt;

provided that:

- a) when R¹ is Me and R² is OMe; then R³ is H; and the combination R⁴, R⁵, and R⁵ is 3,5-di-Me, 3,5-di-OMe-4-Me, 3,5-di-Cl, or 3,5-di-F;
- b) when R^1 is Me and R^2 is OEt; then R^3 is H and the combination R^4 , R^5 , and R^6 is 3,5-di-Me, 3,5-di-OMe-4-Me, 3,5-di-Cl, 3,5-di-F, 2,4- or 2,5-di-F, 2,4- or 2,5-di-Cl;
- c) when R¹ is Et and R² is OMe or OEt; then R³ is H and the combination R⁴, R⁵, and R⁶ is:
 - i) 3,5-di-OMe-4-Me, 3,5-di-Cl, 3,5-di-F, 2,4- or 2,5-di-F, 2,4- or 2,5-di-Cl,
 3-OMe, 2-Cl-5-Me, 2-Br-5-Me, 2-Cl, 2-Br, or 3-Me; or
 - ii) R⁶ is H, R⁴ is Me, and R⁵ is Et, F, Cl, Br, formyl, CF₃, CHF₂, CHCl₂, CH₂F, CH₂Cl, CH₂OH, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, OMe, OEt, SMe, or SEt;
- d) when R¹ is i-Pr; then R² is OMe, or OEt; R³ is H; and the combination R⁴, R⁵, and R⁵ is 3,5-di-Me;
- e) when R³ is Et; then R² is H, R¹ is F or Cl, and the combination R⁴, R⁵, and R⁶ is 3,5-di-Me;
- f) when R² and R³, together with the phenyl carbons to which they are attached, form an ethylenedioxy ring; then R¹ is Me or Et and the combination R⁴, R⁵, and R⁶ is 3,5-di-Me;
- g) when R² and R³, together with the phenyl carbons to which they are attached, form a dihydrofuryl or dihydropyryl ring; then R¹ is Et and the combination R⁴, R⁵, and R⁶ is 3,5-di-Me;
- h) when R¹ is formyl, CF₃, CHF₂, CHCl₂, CH₂F, CH₂Cl, CH₂OH, CH₂OMe, CH₂CN, CN, C=CH, 1-propynyl, 2-propynyl, vinyl, OH, cyclopropyl, CF₂CF₃, CH=CHCN, allyl, azido, SCN, or SCHF₂;

then R² is OMe or OEt, R³ is H, and the combination R⁴, R⁵, and R⁶ is 3,5-di-Me; and

i) when R² is Me, Et, n-Pr, i-Pr, formyl, CF₃, CHF₂, CHcl₂, CH₂F, CH₂Cl, CH₂OH, CH₂OMe, CH₂CN, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, Ac, F, Cl, OH, O-n-Pr, OAc, NMe₂, NEt₂, SMe, SEt, SOCF₃, OCF₂CF₂H, COEt, cyclopropyl, CF₂CF₃, CH=CHCN, allyl, azido, OCF₃, OCHF₂, O-i-Pr, SCN, SCHF₂, SOMe, or NH-CN;

then R¹ is Et, R³ is H, the combination R⁴, R⁵, and R⁶ is 3,5-di-Me; wherein the cells of the subject contain:

- a) an ecdysone receptor complex comprising:
 - 1) a DNA binding domain;
 - 2) a binding domain for the ligand; and
 - 3) a transactivation domain; and
- b) a DNA construct comprising:
 - 1) the exogenous gene; and
 - 2) a response element; and

wherein:

- a) the exogenous gene is under the control of the response element; and
- b) binding of the DNA binding domain to the response element in the presence of the ligand results in activation or suppression of the gene.

Claim 4 (original) A method for producing a polypeptide comprising the steps of:

 a) selecting a cell which is substantially insensitive to exposure to a ligand of the formula:

$$\mathbb{R}^{8} \xrightarrow{\mathbb{R}^{2}} \mathbb{R}^{1}$$

wherein:

E is a (C₄-C₆)alkyl containing a tertiary carbon or a cyano(C₈-C₅)alkyl containing a tertiary carbon;

- R¹ is H, Me, Et, i-Pr, F, formyl, CF₂, CHF₂, CHCl₂, CH₂F, CH₂Cl, CH₂OH, CH₂OMe, CH₂CN, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, OH, OMe, OEt, cyclopropyl, CF₂CF₃, CH=CHCN, allyl, azido, SCN, or SCHF₂;
- R² is H, Me, Et, n-Pr, i-Pr, formyl, CF₃, CHF₂, CHCl₂, CH₂F, CH₂Cl, CH₂OH, CH₂OMe, CH₂CN, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, Ac, F, Cl, OH, OMe, OEt, O-n-Pr, OAc, NMe₂, NEt₂, SMe, SEt, SOCF₃, OCF₂CF₂H, COEt, cyclopropyl, CF₂CF₃, CH=CHCN, allyl, azido, OCF₃, OCHF₂, O-i-Pr, SCN, SCHF₂, SOMe, NH-CN, or joined with R³ and the phenyl carbons to which R² and R³ are attached to form an ethylenedioxy, a dihydrofuryl ring with the oxygen adjacent to a phenyl carbon, or a dihydropyryl ring with the oxygen adjacent to a phenyl carbon;
- R³ is H, Et, or joined with R² and the phenyl carbons to which R² and R³ are attached to form an ethylenedioxy, a dihydrofuryl ring with the oxygen adjacent to a phenyl carbon, or a dihydropyryl ring with the oxygen adjacent to a phenyl carbon;
- R⁴, R⁵, and R⁶ are independently H, Me, Et, F, Cl, Br, formyl, CF₃, CHF₂, CHCl₂, CH₂F, CH₂Cl, CH₂OH, CN, CCH, 1-propynyl, 2-propynyl, vinyl, OMe, OEt, SMe, or SEt;

provided that:

- a) when R¹ is Me and R² is OMe; then R³ is H; and the combination R⁴, R⁵, and R⁶ is 3,5-di-Me, 3,5-di-OMe-4-Me, 3,5-di-Cl, or 3,5-di-F;
- b) when R¹ is Me and R² is OEt; then R³ is H and the combination R⁴, R⁵, and R⁶ is 3,5-di-Me, 3,5-di-OMe-4-Me, 3,5-di-Cl, 3,5-di-F, 2,4- or 2,5-di-F, 2,4- or 2,5-di-Cl;
- c) when R¹ is Et and R² is OMe or OEt; then R³ is H and the combination R⁴, R⁵, and R⁶ is:
 - i) 3,5-di-OMe-4-Me, 3,5-di-Cl, 3,5-di-F, 2,4- or 2,5-di-F, 2,4- or 2,5-di-Cl, 3-OMe, 2-Cl-5-Me, 2-Br-5-Me, 2-Cl, 2-Br, or 3-Me; or
 - ii) R⁶ is H, R⁴ is Me, and R⁵ is Et, F, Cl, Br, formyl, CF₃, CHF₂, CHCl₂,
 CH₂F, CH₂Cl, CH₂OH, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, OMe,
 OEt, SMe, or SEt;

- d) when R¹ is i-Pr;
 then R² is OMe, or OEt; R³ is H; and the combination R⁴, R⁵, and R⁶ is 3,5-di-Me;
- e) when R³ is Et; then R² is H, R¹ is F or Cl, and the combination R⁴, R⁵, and R⁶ is 3,5-di-Me;
- f) when R² and R³, together with the phenyl carbons to which they are attached, form an ethylenedioxy ring; then R¹ is Me or Et and the combination R⁴, R⁵, and R⁶ is 3,5-di-Me;
- g) when R² and R³, together with the phenyl carbons to which they are attached, form a dihydrofuryl or dihydropyryl ring; then R¹ is Et and the combination R⁴, R⁵, and R⁶ is 3,5-di-Me;
- h) when R¹ is formyl, CF₃, CHF₂, CHcl₂, CH₂F, CH₂Cl, CH₂OH, CH₂OMe, CH₂CN, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, OH, cyclopropyl, CF₂CF₃, CH=CHCN, allyl, azido, SCN, or SCHF₂;
 then R² is OMe or OEt, R³ is H, and the combination R⁴, R⁵, and R⁵ is 3,5-di-Me; and
- i) when R² is Me, Et, n-Pr, i-Pr, formyl, CF₃, CHF₂, CHCl₂, CH₂F, CH₂Cl, CH₂OH, CH₂OMe, CH₂CN, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, Ac, F, Cl, OH, O-n-Pr, OAc, NMe₂, NEt₂, SMe, SEt, SOCF₃, OCF₂CF₂H, COEt, cyclopropyl, CF₂CF₃, CH=CHCN, allyl, azido, OCF₃, OCHF₂, O-i-Pr, SCN, SCHF₂, SOMe, or NH-CN;

then R1 is Et, R3 is H, the combination R4, R6, and R6 is 3,5-di-Me;

- b) introducing into the cell:
 - 1) a DNA construct comprising:
 - a) an exogenous gene encoding the polypeptide; and
 - b) a response element; wherein the gene is under the control of the response element; and
 - 2) an ecdysone receptor complex comprising:
 - a) a DNA binding domain;
 - b) a binding domain for the ligand; and
 - e) a transactivation domain; and

c) exposing the cell to the ligand.

Claim 5 (previously presented) A method for regulating endogenous or heterologous gene expression in a transgenic organism, wherein the organism is other than plant, comprising contacting a ligand of the formula:

$$\mathbb{R}^3$$
 \mathbb{R}^2
 \mathbb{R}^1
 \mathbb{R}^4
 \mathbb{R}^5

wherein:

E is a (C₄-C₆)alkyl containing a tertiary carbon or a cyano(C₈-C₅)alkyl containing a tertiary carbon;

R¹ is H, Me, Et, i-Pr, F, formyl, CF₃, CHF₂, CHCl₂, CH₂F, CH₂Cl, CH₂OH, CH₂OMe, CH₂CN, CN, C=CH, 1-propynyl, 2-propynyl, vinyl, OH, OMe, OEt, cyclopropyl, CF₂CF₃, CH=CHCN, allyl, azido, SCN, or SCHF₂;

R² is H, Me, Et, n-Pr, i-Pr, formyl, CF₃, CHF₂, CHCl₂, CH₂F, CH₂Cl, CH₂OH, CH₂OMe, CH₂CN, CN, C=CH, 1-propynyl, 2-propynyl, vinyl, Ac, F, Cl, OH, OMe, OEt, O-n-Pr, OAc, NMe₂, NEt₂, SMe, SEt, SOCF₃, OCF₂CF₂H, COEt, cyclopropyl, CF₂CF₃, CH=CHCN, allyl, azido, OCF₃, OCHF₂, O-i-Pr, SCN, SCHF₂, SOMe, NH-CN, or joined with R³ and the phenyl carbons to which R² and R³ are attached to form an ethylenedioxy, a dihydrofuryl ring with the oxygen adjacent to a phenyl carbon, or a dihydropyryl ring with the oxygen adjacent to a phenyl carbon;

R³ is H, Et, or joined with R² and the phenyl carbons to which R² and R³ are attached to form an ethylenedioxy, a dihydrofuryl ring with the oxygen adjacent to a phenyl carbon, or a dihydropyryl ring with the oxygen adjacent to a phenyl carbon;

R⁴, R⁵, and R⁶ are independently H, Me, Et, F, Cl, Br, formyl, CF₈, CHF₂, CHCl₂, CH₂F, CH₂Cl, CH₂OH, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, OMe, OEt, SMe, or SEt;

provided that:

a) when R1 is Me and R2 is OMe;

then R³ is H; and the combination R⁴, R⁵, and R⁶ is 3,5-di-Me, 3,5-di-OMe-4-Me, 3,5-di-Cl, or 3,5-di-F;

- b) when R¹ is Me and R² is OEt; then R⁸ is H and the combination R⁴, R⁵, and R⁶ is 3,5-di-Me, 3,5-di-OMe-4-Me, 3,5-di-Cl, 3,5-di-F, 2,4- or 2,5-di-F, 2,4- or 2,5-di-Cl;
- c) when R¹ is Et and R² is OMe or OEt; then R³ is H and the combination R⁴, R⁵, and R⁶ is:
 - i) 3,5-di-OMe-4-Me, 3,5-di-Cl, 3,5-di-F, 2,4- or 2,5-di-F, 2,4- or 2,5-di-Cl, 3-OMe, 2-Cl-5-Me, 2-Br-5-Me, 2-Cl, 2-Br, or 3-Me; or
 - ii) R⁶ is H, R⁴ is Me, and R⁵ is Et, F, Cl, Br, formyl, CF₃, CHF₂, CHCl₂,
 CH₂F, CH₂Cl, CH₂OH, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, OMe,
 OEt, SMe, or SEt;
- d) when R¹ is i-Pr;
 then R² is OMe, or OEt; R³ is H; and the combination R⁴, R⁵, and R⁶ is 3,5-di-Me;
- e) when R³ is Et; then R² is H, R¹ is F or Cl, and the combination R⁴, R⁵, and R⁵ is 3,5-di-Me;
- f) when R² and R³, together with the phenyl carbons to which they are attached, form an ethylenedioxy ring; then R¹ is Me or Et and the combination R⁴, R⁵, and R⁶ is 3,5-di-Me;
- g) when R² and R³, together with the phenyl carbons to which they are attached, form a dihydrofuryl or dihydropyryl ring; then R¹ is Et and the combination R⁴, R⁵, and R⁶ is 3,5-di-Me;
- h) when R¹ is formyl, CF₃, CHF₂, CHCl₂, CH₂F, CH₂Cl, CH₂OH, CH₂OMe, CH₂CN, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, OH, cyclopropyl, CF₂CF₃, CH=CHCN, allyl, azido, SCN, or SCHF₂; then R² is OMe or OEt, R³ is H, and the combination R⁴, R⁵, and R⁶ is 3,5-di-Me; and
- i) when R² is Me, Et, n-Pr, i-Pr, formyl, CF₃, CHF₂, CHcl₂, CH₂F, CH₂Cl, CH₂OH, CH₂OMe, CH₂CN, CN, C≡CH, 1-propynyl, 2-propynyl, vinyl, Ac, F. Cl. OH, O-n-Pr, OAc, NMe₂, NEt₂, SMe, SEt, SOCF₃, OCF₂CF₂H,

COEt, cyclopropyl, CF₂CF₃, CH=CHCN, allyl, azido, OCF₃, OCHF₂, O-i-Pr, SCN, SCHF₂, SOMe, or NH-CN;

then R¹ is Et, R³ is H, the combination R⁴, R⁵, and R⁶ is 3,5-di-Me; with an ecdysone receptor complex within the cells of the organism wherein the cells further contain a DNA binding sequence for the ecdysone receptor complex when in combination with the ligand and wherein formation of an ecdysone receptor complex-ligand-DNA binding sequence complex induces expression of the gene.

Claim 6 (cancelled)

Claim 7 (original) The method of Claim 3 wherein the ligand is of the specified formula and E is t-butyl; R¹ is Me, Et, i-Pr, or F; R² is OH, OMe, OEt, or joined with R³ and the phenyl carbons to which R² and R³ are attached to form an ethylenedioxy or dihydrofuryl ring with the oxygen adjacent to a phenyl carbon; R³ is H, Et or joined with R² and the phenyl carbons to which R² and R³ are attached to form an ethylenedioxy or dihydrofuryl ring with the oxygen adjacent to a phenyl carbon; and R⁴, R⁵, and R⁶ are independently Me, F, Cl, CH₂OH, or OMe.

Claim 8 (original) The method of Claim 4 wherein the ligand is of the specified formula and E is t-butyl; R¹ is Me, Et, i-Pr, or F; R² is OH, OMe, OEt, or joined with R³ and the phenyl carbons to which R² and R³ are attached to form an ethylenedioxy or dihydrofuryl ring with the oxygen adjacent to a phenyl carbon; R⁸ is H, Et or joined with R² and the phenyl carbons to which R² and R³ are attached to form an ethylenedioxy or dihydrofuryl ring with the oxygen adjacent to a phenyl carbon; and R⁴, R⁵, and R⁶ are independently Me, F, Cl, CH₂OH, or OMe.

Claim 9 (original) The method of Claim 5 wherein the ligand is of the specified formula and E is t-butyl; R¹ is Me, Et, i-Pr, or F; R² is OH, OMe, OEt, or joined with R³ and the phenyl carbons to which R² and R³ are attached to form an ethylenedioxy or dihydrofuryl ring with the oxygen adjacent to a phenyl carbon; R³ is H, Et or joined with R² and the phenyl carbons to which R² and R³ are attached to form an ethylenedioxy or dihydrofuryl ring with the oxygen adjacent to a phenyl carbon; and R⁴, R⁵, and R⁶ are independently Me, F, Cl, CH₂OH, or OMe.

Claim 10 (cancelled)

Claim 11 (original) The method of Claim 3 wherein the ligand is of the specified formula and E is t-butyl, R¹ is Et, R² is OEt, R³ is H, and the combination R⁴, R⁵, and R⁶ is 3,5-di-Me.

Claim 12 (original) The method of Claim 4 wherein the ligand is of the specified formula and E is t-butyl, R^1 is Et, R^2 is OEt, R^3 is H, and the combination R^4 , R^5 , and R^6 is 3,5-di-Me.

Claim 13 (original) The method of Claim 5 wherein the ligand is of the specified formula and E is t-butyl, R¹ is Et, R² is OEt, R³ is H, and the combination R⁴, R⁵, and R⁶ is 3,5-di-Me.

Claim 14 (cancelled)

Claim 15 (original) The method of Claim 3 wherein the ecdysone receptor complex is a chimeric ecdysone receptor complex and the DNA construct further comprises a promoter.

Claim 16 (original) The method of Claim 4 wherein the ecdysone receptor complex is a chimeric ecdysone receptor complex and the DNA construct further comprises a promoter.

Claim17 (original) The method of Claim 5 wherein the ecdysone receptor complex is a chimeric ecdysone receptor complex and the DNA construct further comprises a promoter.

Claim 18 (cancelled)

Claim 19 (original) The method of Claim 3 wherein the subject is a mammal.

Claim 20 (previously presented) The method of Claim 3 wherein the subject is a fungus or yeast.

In view of the foregoing amendments, Applicants submit that the "Amendments to the Claims" is in compliance with 37 CFR § 1.121.2

Respectfully submitted,

Camille Johy-Tornetta, Ph.D. Registration No. 48,592

RheoGene, Inc. 2650 Eisenhower Avenue Norristown, PA 19403 Telephone: (610) 650-8734 Fax: (610) 650-8755

Date: March 7, 2005

This Page is Inserted by IFW Indexing and Scanning Operations and is not part of the Official Record

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

□ BLACK BORDERS
 □ IMAGE CUT OFF AT TOP, BOTTOM OR SIDES
 □ FADED TEXT OR DRAWING
 □ BLURRED OR ILLEGIBLE TEXT OR DRAWING
 □ SKEWED/SLANTED IMAGES
 □ COLOR OR BLACK AND WHITE PHOTOGRAPHS
 □ GRAY SCALE DOCUMENTS
 □ LINES OR MARKS ON ORIGINAL DOCUMENT
 □ REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY

IMAGES ARE BEST AVAILABLE COPY.

OTHER:

As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.